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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,440	03/26/2004	Ikuo Matsui	13558-002002	8967

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EXAMINER

PAK, YONG D

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/810,440

Applicant(s)

MATSUI ET AL.

Examiner

Yong D Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This application is a divisional of 09/967,645, which is now abandoned.

The preliminary amendment filed on March 26, 2004, canceling claims 1-35 and adding claims 36-38, has been entered.

Claims 36-38 are pending and are under consideration.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-38 recite the phrase "a substrate comprising an aromatic amino acid and an α -keto acid". It is unclear to the Examiner whether the substrate is drawn to one substrate comprising an aromatic amino acid moiety and an α -keto acid moiety or

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whether the substrates for the enzyme comprises of two separate substrates, an aromatic amino acid and an α -keto acid.

Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-38 are drawn to a method of obtaining an amine by contacting an amino acid and an α -keto acid with an aminotransferase. However, the product of such a reaction is a ketone and an amino acid. It is unclear to the Examiner if the method involves a step of separating these products by any means such that a single product is purified or if the method is directed to always obtaining a mixture of these products. In the context of the above, Examiner takes the position that these claims are incomplete for omitting essential steps, such omission amounting to a gap between the steps and these claims are incomplete for omitting essential elements, such omission amounting to a gap between the elements. The omitted steps are: steps in converting or separating the end products, ketone and amino acid, of the aminotransferase reaction to an amine. The omitted elements are: enzymes or chemical agents necessary to convert or separate the end products, ketone and amino acid, of the aminotransferase reaction to an amine.

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Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 recites the phrase "having one or more deletions, replacements or additions". It is unclear to the Examiner what is being deleted, replaced or added, i.e. amino acids, amino groups, carboxyl groups or other elements of the enzyme. It appears that applicant meant to recite one or more amino acid of SEQ ID NO:1. If that is so, amending the claim accordingly would overcome the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 36-37 are drawn to a method of obtaining an amino acid, amine or prochiral ketone by using any polypeptide comprising an N-terminal amino acid sequence of amino acid at position 2 through 25 of SEQ ID NO:1, wherein the polypeptide has aminotransferase activity, derived from any source, and has the properties recited in the claims, such as optimum pH, bioelectric point, etc. Amino acids

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2-25 of SEQ ID NO:1 amounts to only 6% of the whole structure of SEQ ID NO:1 and lacks any catalytic or substrate binding domain. Therefore, these claims are drawn to a genus of polypeptides having any structure except for the short N-terminal region of 24 amino acids. A description of only 24 amino acid is not enough to describe the whole genus comprising any aminotransferase. The specification only teaches one species, the aminotransferase having the full length amino acid sequence of SEQ ID NO:1. One species is not enough to describe the whole genus and there is no evidence on the record of the relationship between the structure of the aminotransferase of SEQ ID NO:1 and the structure of any aminotransferase comprising amino acids 2-25 of SEQ ID NO:1. Therefore, the specification fails to describe a representative species of the genus of polypeptides comprising any aminotransferase.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 36-37.

Claims 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 38 is drawn to a method of obtaining an amino acid, amine or prochiral ketone by using an aminotransferase of SEQ ID NO:1 having one or more amino acid

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deletions, replacements or additions. Since there is no limit to structure or source of the polypeptide, the claim encompasses a genus of molecules described by the function as being an aminotransferase. The specification only teaches one species, the aminotransferase having the amino acid sequence of SEQ ID NO:1. One species is insufficient to describe the whole genus containing a vast number and combinations of amino acid deletions, replacements or additions. The specification fails to place limitations on the aminotransferase structure or disclose which amino acid(s) of SEQ ID NO:1 can be safely modified and still impart aminotransferase activity. Therefore, the specification fails to describe other representative species from other sources or by identifying characteristics or structural properties other than the functionality of being an aminotransferase.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 36-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of obtaining an glutamic acid using a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and 2-ketoglutaric acid as its substrate, does not reasonably provide enablement for a method of obtaining any or all amino acid or prochiral ketone using any aminotransferase having amino acids 2-25 of SEQ ID NO:1 as the N-terminal amino acids or a aminotransferase of SEQ ID NO:1 having one or more amino acid deletions, replacements or additions. The

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specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 36-37 are drawn to a method of obtaining any amino acid, amine or prochiral ketone by using any polypeptide comprising an N-terminal amino acid sequence of amino acid at position 2 through 25 of SEQ ID NO:1, wherein the polypeptide has aminotransferase activity, derived from any source, and has the properties recited in the claims, such as optimum pH, bioelectric point, etc. Amino acids 2-25 of SEQ ID NO:1 amounts to only 6% of the whole structure of SEQ ID NO:1 and lacks any catalytic or substrate binding domain. Claim 38 is drawn to a method of obtaining an amino acid, amine or prochiral ketone by using an aminotransferase of SEQ ID NO:1 having one or more amino acid deletions, replacements or additions. Therefore, these claims are drawn to polypeptides having unlimited structure. Further more, these claims are drawn to a method of obtaining any amino acids, amine or

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prochiral ketone even though the specification is limited to the teaching and making of only glutamic acid.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides having aminotransferase activity broadly encompassed in the method of the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a method of obtaining an amino acid, amine or prochiral ketone using an aminotransferase having the amino acid sequence of SEQ ID NO:1.

It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of polypeptide comprising the amino acid sequence of SEQ ID NO:1 but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and variants of any aminotransferase or modifications of the aminotransferase of SEQ ID NO:1 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting aminotransferase activity; (B) the general tolerance of aminotransferase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue (up to 100% of the amino acids of SEQ ID NO:1) with an expectation of obtaining the desired biological function; (D) a rational and predictable scheme for making any amino acid using the above amino transferase; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of using any aminotransferase

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comprising amino acids 2-25 of SEQ ID NO:1 and aminotransferases with an enormous number of amino acid modifications of the aminotransferase of SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of an aminotransferase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Warren et al.

Claim 38 is drawn to a method of obtaining an amino acid, amine or prochiral ketone comprising contacting an aminotransferase having the amino acid sequence of SEQ ID NO:1 comprising one or more amino acids deletions, replacements or additions with an aromatic amino acid and an α -keto acid.

Warren et al. (U.S. Patent No. 5,814,473 - form PTO-892) teaches a method of obtaining an amino acid, amine or prochiral ketone comprising contacting an

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aminotransferase with an aromatic amino acid and an α -keto acid (Columns 1-2). Since applicants have not placed any limitations in the amino acid changes, the aminotransferase of Warren et al. reads on an aminotransferase of SEQ ID NO:1 comprising one or more amino acid deletions, replacements or additions. Therefore, Warran et al. anticipates claim 38.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections, set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-37 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kawarabayasi et al. and Warren et al.

Claims 36-37 are drawn to a method of obtaining an amino acid, amine or prochiral ketone comprising contacting an aminotransferase comprising amino acids 2-25 of SEQ ID NO:1 with an aromatic amino acid and an α -keto acid.

Kawarabayasi et al. (form PTO 892) teaches an aminotransferase that is 100% identical to SEQ ID NO:1 of the instant invention and therefore comprises amino acids 2-25 of SEQ ID NO:1 (pages 56-59 and 65 and see Sequence Alignment – form PTO-892). The aminotransferase of Kawarabayasi et al. is from a thermophilic bacterium (abstract). The aminotransferase of Kawarabayasi et al. inherently possesses the same material structure and functional characteristics as the aminotransferase of claims 36-37 since the aminotransferase of Kawarabayasi et al. and the aminotransferase of the instant invention are the same enzyme. Further, this enzyme's inherent function is to transfer amino groups. From the teaching of Kawarabayasi et al., one having ordinary skill in the art would have recognized to use the enzyme of Kawarabayasi et al. to make amino acids.

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In the alternative, combining the teachings Kawarabayasi et al. with that of Warren et al., it would have been obvious to one having ordinary skill in the art to use the aminotransferase of Kawarabayasi et al. to make amino acids using the method of Warrant et al., as discussed above. One having ordinary skill in the art would have been motivated to use the aminotransferase of Kawarabayasi et al. since enzymes isolated from thermophilic organisms have high thermostability and higher optimum temperature, which are advantageous in making products in an industrial scale. One of ordinary skill in the art would have had a reasonable expectation of success since Kawarabayasi et al. teaches an aminotransferase having an amino acid sequence that is 100% identical to the instant aminotransferase and Warren et al. successfully teach a method of obtaining an amino acid and prochiral ketone by contacting an amino acid and an α -keto acid with an aminotransferase.

Therefore, the above references render claims 36-37 *prima facie* obvious to one of ordinary skill in the art.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

A handwritten signature in black ink, appearing to read 'Manjunath Rao', with a stylized flourish at the end.

Manjunath Rao
Primary Examiner 1652